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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/950,003

09/12/2001

Pasqua Oreste

MARGI 27 P1

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7590

03/26/2008

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EXAMINER

KRISHNAN, GANAPATHY

ART UNIT

PAPER NUMBER

1623

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DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/950,003	<b>Applicant(s)</b> ORESTE ET AL.	
	<b>Examiner</b> Ganapathy Krishnan	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 15-22, 24, 25, 27-34, 38-53, 56-62, 64, 66, 68 and 70 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15-22, 24, 25, 27-34, 38-53, 56-62, 64, 66, 68 and 70 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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### **DETAILED ACTION**

The After Final Amendment filed 11/30/2007 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1-14, 23, 26, 35-37, 54-55, 63, 65, 67, 69 and 71-77 have been canceled.
2. Claims 15-17, 20 and 24 have been amended.
3. Remarks drawn to priority claims and rejections under obviousness-type double patenting.

Claims 15-22, 24-25, 27-34, 38-53, 56-62, 64, 66, 68 and 70 are pending in the case.

The Finality of the Office Action mailed 5/31/2007 has been **withdrawn** since claims 16, 18-19, 23, 25-34, 38-53, 56-62, 64, 68 and 70 were inadvertently indicated as rejected even though their rejection in the Non-Final Action of 9/14/2006 was indicated as being rendered moot. The following rejections are made of record.

### ***Priority***

Applicants have acknowledged that the priority to the Italian Application MI2000A00065 has been denied and are not formally withdrawing the priority claim so as to maintain continuity for the priority claim in copending divisional Application No. 11/030,156. The denial of priority is being maintained till a formal withdrawal is filed.

### ***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

The rejection of Claims 38-62 under 35 U.S.C. 101 as claiming the same invention as that of claims 14-36 of copending Application No. 11/030156 ('156 application) has been rendered moot by cancellation of claims 14-36 in the '156 application.

The following new statutory type double patenting rejection is made of record.

Claims 17-19, 50-53 and 59-62 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 19-21, 49-52 and 56-59 of copending Application No. 11/440,749 ('749).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined

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application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-22, 24-25 and 27-34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4-6, 9-10 of copending Application No. 11/030156 ('156). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant claims 15-17 are drawn to a process for the synthesis of K5 glycosaminoglycans comprising the steps of N-deacetylation, N-sulfation; C5 epimerization of carboxyl group; oversulfation, selective O-desulfation, optional 6-O-sulfation and N-sulfation, in which the selective O-desulfation is done with methanol/DMSO mixture for a period of about 150 minutes. Instant claim 16 is same as claim 15 but the last step is performed at 60°C. Instant claim 17 is also drawn to preparation of K5 glycosaminoglycan with additional steps drawn to 6-O-sulfation and N-sulfation and depolymerization. Dependent claims 18-22, 25-25 and 27-34 recite limitations drawn to reagents used in the various steps.

Claim 4-6, 9-10 of '156 is drawn to a process for the synthesis of K5 polysaccharide using the same process steps with some of the reagents being the same.

Claims 4-6, 9-10 of '156 differ from the instant claims in that the instant claims employ a mixture of methanol/DMSO for a period of about 150 minutes in the selective O-desulfation step. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the process steps could be successfully employed in the method of '156 and vice versa.

In determining the differences between the prior art and the claims, the question is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). In the instant case, '156 teaches performing each of the steps applicant claims. Although the claims of '156 employ a mixture of methanol/DMSO for a certain period of time and a few extra steps like depolymerization, one of ordinary skill in the art would readily recognize that the scheme taught by '156 could be employed in the instant process. One of ordinary skill in the art is seen as one having a PhD in the field of synthesis. The use of known members of classes of reagents in reactions to effectuate the similar modifications taught in the prior art is not seen to render the instantly claimed method unobvious over the art. Once the general reaction has been shown to be old, the burden is on the applicant to present reason or authority for believing that a

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slight alteration in the conditions or structure would affect the basic reaction and thus alter the nature of the product or the operability of the process and thus the unobviousness of the method of producing it.

The following new double patenting rejection is made of record.

Claims 15-16, 20-22, 24-25, 27-34, 38-49, 56-58, 64, 66, 68 and 70 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7, 13-74 of Application No. 11/440,749 ('749). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant claims 15-16, 20-22, 24-25, 27-34, 38-49, 56-58, 64, 66, 68 and 70 are drawn to a process for the synthesis of K5 glycosaminoglycans comprising the steps of N-deacetylation, N-sulfation; C5 epimerization of carboxyl group; oversulfation, selective O-desulfation, optional 6-O-sulfation and N-sulfation, in which the selective O-desulfation is done with methanol/DMSO mixture for a period of about 150 minutes, with dependent claims drawn to various reagents and conditions to be used in the said process, pharmaceutical compositions of product of formula I and method of use of the compounds of formula I.

Claims 7, 13-74 of '749 are also drawn to a process for the synthesis of K5 polysaccharide using the similar process steps with some of the reagents being the same and also compositions of compounds with formula I and their methods of use.

Claims 7, 13-74 of '749 differ from the instant claims in that the instant claims employ a mixture of methanol/DMSO for a period of about 135-165 minutes in the selective O-desulfation step and the claims of '749 drawn to compositions of formula I and their methods of

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use recite a percentage of about 15 to about 35% for R<sub>1</sub>. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the process steps as instantly claimed and the compounds of formula I and their compositions could be successfully employed in the process and methods of '749 and vice versa.

In determining the differences between the prior art and the claims, the question is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). In the instant case, '749 teaches performing each of the steps applicant claims. Although the claims of '749 employ a mixture of methanol/DMSO for a period of time that is wider than the instant and also a slight variation in the percentage of one of the substitutions of the compound of formula I, one of ordinary skill in the art would readily recognize that the scheme taught by '749 could be employed in the instant process and methods. One of ordinary skill in the art is seen as one having a PhD in the field of synthesis. The use of known members of classes of reagents in reactions to effectuate the similar modifications taught in the prior art is not seen to render the instantly claimed method unobvious over the art. Once the general reaction has been shown to be old, the burden is on the applicant to present reason or authority for



believing that a slight alteration in the process conditions or substitution percentage would affect the basic reaction and thus alter the nature of the product or the operability of the process and thus the unobviousness of the method of producing it.

The rejection of Claims 14, 15, 17, 20-22 and 24 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4-6 and 10 of copending Application No. 10/240606 ('606 application) is being maintained for reasons of record.

***Response to Applicants arguments***

According to applicants instant claim 15 is the only claim to which the obviousness type double patenting rejection over claims 4-6 and 10 of copending application 10/240,606 ('606) advanced in the previous action applies and have traversed this rejection, arguing that:

1. The essential feature of instant claim 15 is a process wherein the O-desulfation is carried out for a about 150 minutes. The '606 application discloses a broad range of time periods for the selective O-desulfation step. No preferred range is given. There is no suggestion that the duration affects the structure or the antithrombotic activity of the product obtained. There is no motivation to employ a period of 150 minutes.

3. The Declaration by Oreste shows unexpected results are obtained by carrying out the desulfation for 150 minutes. According to the Declaration the depolymerized products obtained by treating for 120 minutes and 180 minutes underwent substantial loss of activity while that obtained by treatment for 150 minutes maintained good activity. The difference in activity level is significant and unexpected.

4. Applicants have also indicated that based on the Declaration of Oreste and the teaching of '606, instant claims 16-22, 24-25, 27-34, 38-53, 56-62, 64, 66, 68 and 70 are also unobvious.

Applicants' arguments are not found to be persuasive.

Tables 2 and 4 in the Declaration show the coagulation parameters for the product obtained and the results for 2.5 hours for the said treatment have been highlighted. If one looks at the results provided for the coagulation parameters in Table 2 of Publication US 2004/0146994 ('994 publication; publication of the 10/240606 application) it can be seen that the coagulation parameters for two hours (closer to the parameters for the instantly claimed 2.5 hours) is close to the parameters of the instant product. Instant claims recite a time period of about 150 minutes. The language of the claim recitation indicates that the time period could be in the more or less than 150 minutes. Moreover, the '994 publication gives examples 1-11 which range from 2 to 4 hours for the said treatment time and it can be seen that depending on the time of the said treatment there is a change in the coagulation parameters. Based on this observation one of ordinary skill in the art would expect the parameters to change with the time period for the said treatment and would look for optimal results with respect to the time period of the said treatment. One of skill in the art also knows well that activity is affected by the position and the number of sulfate groups in the case of glycosaminoglycans and would also expect changes in some or all of the activities of the products. Based on the teaching of the prior art and in general the knowledge of the skilled artisan a change in the activity level of the coagulation parameters is not unexpected. Hence, the results provided in the instant Declaration are not seen as unexpected. The process and the products are thus not seen as different from those of the '606 application.

***Conclusion***

Claims 15-22, 24-25, 27-34, 38-53, 56-62, 64, 66, 68 and 70 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK

/Shaojia Anna Jiang, Ph.D./

Supervisory Patent Examiner, Art Unit 1623